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08/782,590

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/782,590	01/13/97	ROSE	

EXAMINER	
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1642	10

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DATE MAILED: 02/25/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 12/22/97

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~or thirty days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-87 is/are pending in the application.
Of the above, claim(s) 1-68 + 84-87 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 69-83 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-404-496/40517

1. The Amendment filed September 29, 1997 (Paper No. 5), the Amendment filed December 22, 1997 (Paper No. 7) and the Letter filed February 19, 1998 (Paper No. 9) in response to the Office Action of May 23, 1997 (Paper No. 3), Letter (Paper No. 6) and the telephone interview of February 18, 1998 (see Telephone Interview, Paper No.8) are acknowledged and have been entered. Claims 1-87 are pending in the application and Claims 1-68 and 84-87 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 69-87 are currently under prosecution.

2. Applicant's election with traverse of Group XIV, claims 69-83 in Paper No. 5 is acknowledged. The traversal is on the ground(s) that the inventions have not been shown to be independent and the examination of all groups would not impose a serious burden on the examiner. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in Paper No. 3. As to the question of burden of search, the literature search, particularly relevant in this art, is not coextensive and therefore different searches and issues are involved in the examination of each group. Further, Applicant argues that Inventions XIV and XV should be rejoined because both recite a bispecific reagent. The argument has been noted but has not been found persuasive because Invention XIV comprises both a bispecific reagent and a first therapeutic agent, while Invention XV recites only a bispecific reagent and the two groups represent chemically distinct products, obtained by and used in different methods and thus restriction for examination

purposes as indicated is proper. Further, Applicant argues that there is nothing in claims 69-87 which shows that the first therapeutic agent and the first bispecific reagent can be used in methods different than that of claim 1. The argument has been noted but has not been found persuasive because it is clearly disclosed on page 4 of Paper No. 3 that the bispecific reagent and the therapeutic agent can be used in a materially different process.

As drawn to election of species, the traversal in Paper No. 5 is on the grounds that, (a) the examination of all of the members of the markush groups claimed would not represent a serious burden and (b) no response can be made to recitations in the Action of Sections 4-32 as drawn to the allegations of species. The arguments have been noted but have not been found persuasive because (a) the literature search, particularly relevant in this art, is not coextensive and therefore different searches and issues are involved in the examination of each of the species and (b) as disclosed in Section 48 of Paper No. 3, "response to this requirement, to be complete, must include an election of the invention to be examined even though the requirement be traversed. In Paper No. 7 Applicant elects the species of indoxyl-lactam with traverse. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a). In Paper No. 9, the elction of species requirement is traversed for the reasons set forth in Paper No. 5. The argument has been noted but has not been found persuasive for the reasons set forth above. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification

3. The disclosure is objected to because of the following informalities:

A separate section, headed by the title "Brief Description of the Drawings", including a description of each drawing, is required. Correction of the specification is required. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of Specification

The following order or arrangement is preferred in framing the specification and, except for the title of the invention, each of the lettered items should be preceded by the headings indicated below.

(a) Title of the Invention.
(b) Cross-References to Related Applications (if any).
(c) Statement as to rights to inventions made under Federally-sponsored research and development (if any).
(d) Background of the Invention.
    1. Field of the Invention
    2. Description of the Prior Art.
(e) Summary of the Invention.
(f) **Brief Description of the Drawing.**
(g) Description of the Preferred Embodiment(s).
(h) Claim(s).
(i) Abstract of the Disclosure.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and

use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

5. The specification is objected to under 35 USC 112, first paragraph, and Claims 69-83 are rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to make/use a first therapeutic agent and a first bispecific reagent.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

(a) The specification gives no guidance on or exemplification, either *in vitro* or *in vivo*, of making/using a first therapeutic agent being a soluble precipitable material which is adapted to be converted into an insoluble and non-digestible precipitate by the action of a non-mammalian enzyme wherein the first therapeutic agent is selected from the group consisting of peptides, including opio-melanins, or carbohydrates including cellulose, chitosan and chitin, of proteoglycans of synthetic polymers and of indoxyl compounds. The claims as written read on the adaptation of each of the claimed compounds and all members of the classes of compounds (a) to be disposed adjacent to the first target cancer cells (claims 69-83), (b) converted into an insoluble and non-digestible precipitate by the action of a non-mammalian enzyme (claims 69-83), (c) to, upon conversion to a soluble intermediate, be adapted to being converted into the first extra-cellular precipiate, or a soluble reactive intermediate molecule which is adapted to be oxidized and dimerized thereby forming the first extra-

cellular precipitate (claims 74-76). The specification contemplates the use of the therapeutic agent *in vivo* in the treatment of cancer (see page 2, paragraph 1 of the specification). However, the specification does not provide teachings to establish effective dosages or methods of administration of any of the claimed "adapted" moieties or provide any guidance or exemplifcation on how to "adapt" any of the claimed moieties for any of the limitations disclosed above or provide pharmacokinetic data that would provide guidance to one of skill in the art to predict the efficacy of the claimed therapeutic agent with a reasonable expectation of success.

Clearly, the therapeutic agents may be inactivated *in vivo* before producing a therapeutic effect, for example, by proteolytic degradation, immunological activation or due to an inherently short half life. In addition, the therapeutic agent may not otherwise reach the target because it may be absorbed by fluids, cells and tissues where the therapeutic agent has no effect, circulation into the target area may be insufficient to carry the therapeutic agent and a large enough local concentration may not be established. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed therapeutic agent with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed inventions with a reasonable expectation of success. Further, the specification provides no description of how to "adapt" any of the moieties so that they will be converted into an insoluble and non-

digestible precipitate by the action of a non-mammalian enzyme. Applicant has not shown that, for example, peptides which are "adapted" are capable of functioning as that which is being disclosed. it is pointed out that the term "adapted" could be read to encompass a variety of definitions, i.e. chemical modification, deletions, truncations, substitutions conjugation etc..Applicant has not enabled all of these types of modified peptides.

Protein chemistry, which reads on peptide chemistry, is probably one of the most unpredictable areas of biotechnology. For example, replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Burgess et al. J of Cell Bio. 111:2129-2138, 1990. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. Lazar et al. Molecular and Cellular Biology 8:1247-1252 (1988). Similarly it has been shown that a glycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies. See Tao et al., The Journal of Immunology, 143:2595-2601 (1989). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

Further, Applicant has not enabled "adaptations" of all carbohydrates, proteoglycans, synthetic polymers or indoxyl compounds as claimed. Nor has

Applicant given guidance on how to choose those agents that will, upon "adaptation", function as claimed.

Finally, it is not clear from the teaching of the specification that the insoluble, non-digestible and presumably therapeutic precipitate, resulting from the action of the bispecific reagent upon the therapeutic reagent, will remain in the extra-cellular fluid adjacent to the first bispecific reagent, and thus it is not clear that for example, if toxic, the precipitate will not exert its toxic affects on tissues and organs other than those of the first target cancer cells and therefore damage the unprotected host organism.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use a therapeutic agent as claimed. Therefore, undue experimentation would be required to enable the claims.

(b) The specification gives no guidance on or exemplification, either *in vitro* or *in vivo*, of making/using a bispecific reagent which will convert a first therapeutic agent into an insoluble and non-digestible precipitate at the site of the first target cancer cells. The claims are drawn to a targeting agent moiety and a first enzyme moiety, which is a non-mammalian enzyme moiety, which has a substantial affinity for the first antigenic receptor of the first target cancer cells and thus, as broadly written, read on bispecific antibodies with an antigen binding region and a nonmammalian enzyme region for the conversion of a prodrug to a drug used for the treatment of cancer *in vivo*. The record contains insufficient evidence to establish that the claimed product is useful for treating human cancers. It was well known in the art at the time the invention was made

that although antibodies were highly effective as a means of selectively targeting cancer cells, antibody based targeting of therapeutics has proved relatively ineffective in the treatment of solid tumors such as carcinomas. WO 93/17715 specifically teaches that (1) solid tumors are generally impermeable to antibody-sized molecules; (2) that antibodies that enter the tumor mass do not distribute evenly because of the dense packing of tumor cells; and (3) antigen-deficient mutants can escape being killed by the antibody-based therapies and regrow (p. 4, lines 10-37), thus the ability to use the claimed bispecific reagent would be highly unpredictable. Further, the specification does not provide teachings to establish effective dosages or methods of administration of any of the claimed bispecific reagents. In addition, the bispecific reagent may be inactivated *in vivo* before producing a therapeutic effect, for example, by proteolytic degradation, immunological activation or due to an inherently short half life of, the protein In addition, the bispecific reagent may not otherwise reach the target because it may be absorbed by fluids, cells and issues where the therapeutic agent has no effect, circulation into the target area may be insufficient to carry the therapeutic agent and a large enough local concentration may not be established. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed therapeutic agent with a reasonable expectation of success.

In addition, Applicant claims (claim 76) a first therapeutic agent selected from the group including indoxyl-lactam which is cleavable by the first enzyme

moiety of the first bispecific reagent. Clearly, as taught by Taibi (Dissertation Abstracts International, 1996, vol 57, No. 12B, p. 7515) the action of beta lactamase, a nonmammalian enzyme which cleaves lactam antibiotics, is to hydrolyze the cyclic amid bond in beta lactam antibiotics, resulting in the loss of their antibacterial activity (see abstract). Thus, it appears, that the action of the nonmammalian enzyme on the first therapeutic agent is to render it nontherapeutic and clearly, undue experimentation would be required to enable the claims.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use a bispecific agent as that would function as claimed and undue experimentation would be required to enable the claims.

(c) The specification gives no guidance on or exemplification, either *in vitro* or *in vivo*, of making/using a therapeutic agent in which a cell-impermeant chemical is attached to the first therapeutic agent, the cell-impermeant chemical causing the first therapeutic agent to be cell impermeant (claim 71). The record contains insufficient evidence to establish that the claimed product is useful for treating human cancers. The specification gives no guidance on or exemplification of how to choose the agent to be attached to the broadly claimed first therapeutic agent or how or where to attach it. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use a therapeutic agent in which a cell-impermeant chemical is attached to the first therapeutic agent, the cell-impermeant chemical causing the first therapeutic

agent to be cell impermeant that would function as claimed. Therefore, undue experimentation would be required to enable the claims.

(d) The specification gives no guidance on or exemplification, either *in vitro* or *in vivo*, of making/using a therapeutic agent in which a cell-impermeant chemical is attached to the first therapeutic agent, the cell-impermeant chemical causing the first therapeutic agent to be cell impermeant wherein the cell impermeant chemical is selected from the group including materials having molecular weight greater than 1000 daltons (claim 72). Clearly, as broadly written, the claim reads on any chemical that is greater than 1000 daltons and just as clearly, the specification has not taught how to make or use any therapeutic reagent conjugated to any chemical of unlimited molecular weight. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use a therapeutic agent in which a cell-impermeant chemical is attached to the first therapeutic agent wherein the cell impermeant chemical is selected from the group including materials having molecular weight greater than 1000 daltons that would function as claimed. Therefore, undue experimentation would be required to enable the claims.

6. Claims 69-83 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 69-83 are indefinite in the recitation of the phrase "having a first antigenic receptor". The claims are indefinite because it is not clear which of the heterogeneous population of cancers cells "has" a first antigenic receptor.

(b) Claims 69-83 are indefinite because claim 69 recites the phrase "adapted to be converted". The claims are confusing because it is not clear what is meant by the term "adapted". Is the therapeutic agent conjugated to another molecule, is it reduced or oxidized?

(c) Claims 69-83 are indefinite because claim 69 recites the phrase ""the first therapeutic.....when administered.....having a heterogeneous population of cancer cells". The claims are confusing because it is not clear whether the living host or the therapeutic agent has a heterogenous population of cancer cells.

(d) Claims 69-83 are indefinite because claim 69 recites "adapted to be converted". The claims are confusing because neither claim 69 not the claims dependent on claim 69, claims that the first therapeutic agent is converted to a precipitate.

(e) Claims 69-83 are indefinite because it is not clear whether the first therapeutic agent is therapeutic before or after conversion to the insoluble and non-digestible precipitate or whether the therapeutic agent is neutralized or destroyed by the conversion process.

(f) Claims 69-83 are indefinite because claim 69 recites the phrase "adapted to be disposed adjacent". The claims are confusing because it is not clear (as disclosed above) what is meant by the term "adapted". Further, the claims are confusing because the term "disposed" is not defined either in the claims or the specification and therefore the metes and bounds of the patent protection claimed can not be determined. For example, is the therapeutic agent

adapted to be sequestered adjacent to the first target cancer cells, or is it adapted to disintegrate adjacent to the first target cancer cells.

(g) Claims 69-83 are indefinite because claim 69 recites the phrases, "a first therapeutic agent", "first target cells", "first bispecific reagent", "first extracellular precipitate" without reciting any additional moieties.

(h) Claims 69-83 are indefinite because claim 69 recites an improper Markush group. MPEP 706.03(y) provides that the materials set forth in a Markush group ordinarily must belong to a recognized physical class or chemical class or to an art-recognized class.

The members of the Markush groups recited in claim 69 do not belong to a recognized class nor do they function by a common mechanism as therapeutic reagents. The Markush groups of claim 69 recites peptides, carbohydrates, proteoglycans, synthetic polymers and indoxyl compounds. The above embodiments should be set out as separate claims.

(i) Claims 69-83 are indefinite because claim 69 recites, in the improper Markush group disclosed above, the phrases "peptides, including .....", "carbohydrates including .....". The claims are confusing because it is not clear whether the peptides and carbohydrates claimed are limited to those recited in the claim or whether they include other moieties of the same class.

(j) Claims 69-83 are indefinite because claim 69 recites "a first antigenic epitope [being.....". Because there is no closing bracket, it is not possible to determine how much of the remainder of the claim is deleted by amendment.

(k) Claims 69-83 are indefinite because claim 69 recites the phrase "for an extended period of time". The term "extended" is a relative term and is not

defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of "extendedness" and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(l) Claim 72 is indefinite because claim 72 recites the phrase "materials having a molecular weight greater than 1000 daltons. The claim is confusing because the claimed materials are not defined either by the claim or by the specification, thus the metes and bounds of the claims cannot be determined, for example could the materials include a breadbox?.

(m) Claims 74-75 are indefinite because claim 74 recites the phrase "adapted to be naturally converted". The claims are confusing because it is not clear (as disclosed above) what is meant by the term "adapted", thus the metes and bounds of patent protection requested are not defined. Further, the meaning of "naturally converted" is not clear. For example, is the intermediate converted into an extra-cellular precipitate spontaneously or do endogenous molecules precipitate the conversion?

(n) Claims 74-76 are indefinite because it is not clear at what point the intermediate has been adapted to be naturally converted. For example, are the intermediates removed from the system in order to be adapted?

(o) Claim 75 is indefinite because claim 75 recites the phrase "soluble.....adapted to be naturally oxidized". The claims are confusing because it is not clear (as disclosed above) what is meant by the term "adapted", thus the metes and bounds of patent protection requested are not defined. Further, the meaning of "naturally oxidized" is unclear. For example, is the intermediate oxidized spontaneously or do endogenous molecules precipitate the oxidation?

(p) Claim 76 is indefinite in the recitation of the phrase "and the like". The claimed indoxyls include indoxyls not actually disclosed (those encompassed by "and the like") and the scope of the claim is unascertainable. Further, the claim is confusing because the claim recites the phrase "adapted to be oxidized and dimerized". The claim is confusing because it is not clear (as disclosed above) what is meant by the term "adapted", thus the metes and bounds of patent protection requested are not defined.

(q) Claim 77 is indefinite because it recites the phrase "includes a substance". The claim is confusing because it is not clear what substances would alter the characteristics of indoxyl compounds and first extra-cellular precipitates Further, the claim is indefinite in the recitation of the phrase "alters the characteristics of". The claim is confusing because it is not clear what characteristics are being altered, for example are the solubility, oxidizability or cleavability of the molecules being altered.

(r) Claims 78-80, and the claims dependent on said claims, are indefinite in the recitation of the phrase "alters the characteristics of". The claims are confusing because it is not clear what characteristics are being altered, for example are the solubility, oxidizability or cleavability of the molecules being altered.

(s) Claim 79 is indefinite in the recitation of the phrase "derivatives of benzyloxy". The claim is confusing because the term "derivatives" is not defined either in the claim or in the specification.

(t) Claim 82 is indefinite because it recites the phrase "solubilizing effect.....dissipated". The claims are confusing because it is not clear what is

meant by the dissipation of the solubilizing effect. Further, the claim is indefinite in the recitation of the phrase "solubilizing effect" because it is not clear whether the moiety is indeed soluble or insoluble. Further, the claim is confusing in the recitation of the phrase "being adapted to form". The claim is confusing because the term "adapted" is not defined either in the specification of in the claims. Further, the claim is confusing in the recitation of the phrase "the remaining material". It is not clear what is the remaining material, that is, is it the soluble or the insoluble moiety?

(u) Claims 69-83 because claim 69 recites the term "having" because it is not clear whether "having" is open or closed. It is suggested that this language be removed from the claim.

Claim Rejections - 35 USC § 102

7 The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 69-83 are rejected under 35 U.S.C. § 102() as being anticipated by WO9109134 (see attached abstract).

The claims are drawn to a bispecific reagent having a first enzyme moiety which is a nonmammalian enzyme moiety and a second moiety including a targeting agent which has a substantial affinity for the first target cancer cells

and a therapeutic reagent adapted to be converted into an insoluble and non-digestible precipitate by the action of a non-mammalian enzyme. Additional limitations recited in the claims, for example, (a) administration to a living host having a heterogenous population or cancer cells, (b) the description of those cancer cells (c) disposition of the therapeutic agent adjacent to the cancer cells, (d) capability of the therapeutic agent to be converted by the bispecific reagent into an insoluble and non-digestible precipitate by the enzyme, (e) binding of the bispecific reagent to the cancer cells (f) the description of an extracellular precipitate and its epitopes converted from the therapeutic agent and (g) its stay adjacent to the bispecific reagent are intended uses of the bispecific reagent and therapeutic agents (a, c, e, f and g) or inherent properties of the bispecific reagent and therapeutic agents (d) or descriptions of sites of intended use (b), thus these limitations are not given weight in comparing the claim with the prior art. The claims read on the ingredients per se, which are a therapeutic agent and a bispecific reagent.

WO9109134 teaches a bispecific antibody specific for a human cancer cell, e.g. against human transferrin receptor, coupled to a prodrug activating enzyme ,e.g. urokinase or beta-glucuronidase, (both or which were well known in the art at the time the invention was made to be nonmammalian enzymes) which convert inactive glucuronidated cytostatic drugs into active compounds and which are administered to cancer patients to produce selective cytostatic activity on cancer cells (see attached abstract). The reference does not specifically teach that the therapeutic reagents are adapted to be converted into insoluble and non-digestible precipitates. However, the claimed therapeutic

agents appears to be the same as the prior art therapeutic agents, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached at (703) 308-2731. The fax phone number for this Art Unit is (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 USC 132 or which otherwise require a signature may be used by the applicant and should be addressed to lila.feisee@uspto.gov.

All internet e-mail communications will be made of record in the application file. **PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of**

the confidentiality requirements of USC 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
February 23, 1998

LILA FEISEE
SUPERVISORY PATENT EXAMINER
GROUP 1800